(12) UK Patent Application (19) GB (11) 2 228 922 (13) A

(43) Date of A publication 12.09.1990

(21) Application No 9004895.0

(22) Date of filing 05.03.1990

(30) Priority data
(31) 8905017 (32) 04.03.1989 (33) GB

(71) Applicants
Alan John Gordon
30 Menlove Gardens West, Liverpool, L18 2ET, United Kingdom

Kenneth John Harris
66 Olivia Street, Kirkdale, Liverpool, United Kingdom

(72) Inventors
Alan John Gordon
Kenneth John Harris

(74) Agent and/or Address for Service
Roystons
Tower Building, Water Street, Liverpool, L3 1BA, United Kingdom

(51) INT CL[5]
B65D

(52) UK CL (Edition K)
B8P PK10
U1S S1310

(56) Documents cited
GB 2086855 A GB 2079250 A GB 1601885 A
GB 1412977 A EP 0263695 A2 US 4749085 A
US 4318477 A US 4261468 A

(58) Field of search
UK CL (Edition J) B8P PA PAX PK10
INT CL[4] B65D

(54) Packaging drugs

(57) A drug package which enables prescription of drugs at variable levels in a single dose which is clearly prescribed to the user comprises a carrier 5 having a plurality of reception locations (holes 9) disposed in identifiable groupings representing single doses and wherein the groupings are able to accommodate several desired medications. The dose level of discrete medications making up said groups are selected from different available dose levels to build up a prescribed single dose for that grouping. Preferably the discrete medications of a particular dose level are spaced on strips at spacings to suit the spacing of the reception locations.

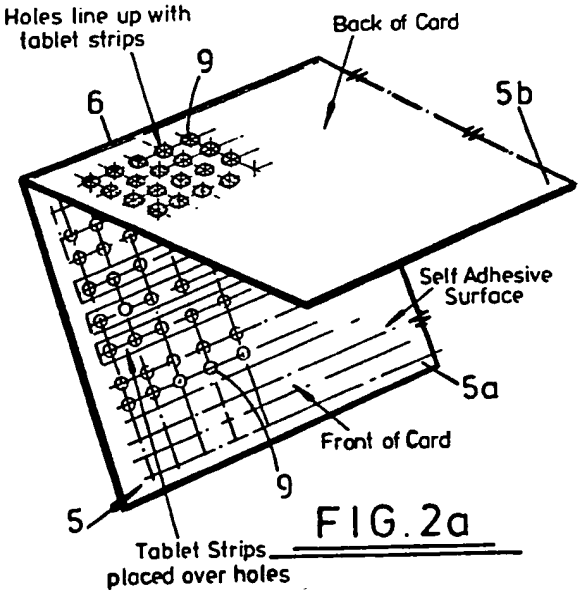


FIG. 2a

At least one drawing originally filed was informal and the print reproduced here is taken from a later filed formal copy.

GB 2 228 922 A

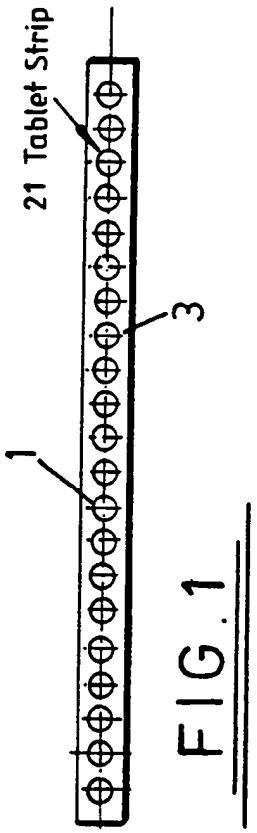

21 Tablet Strip
1
3

FIG. 1

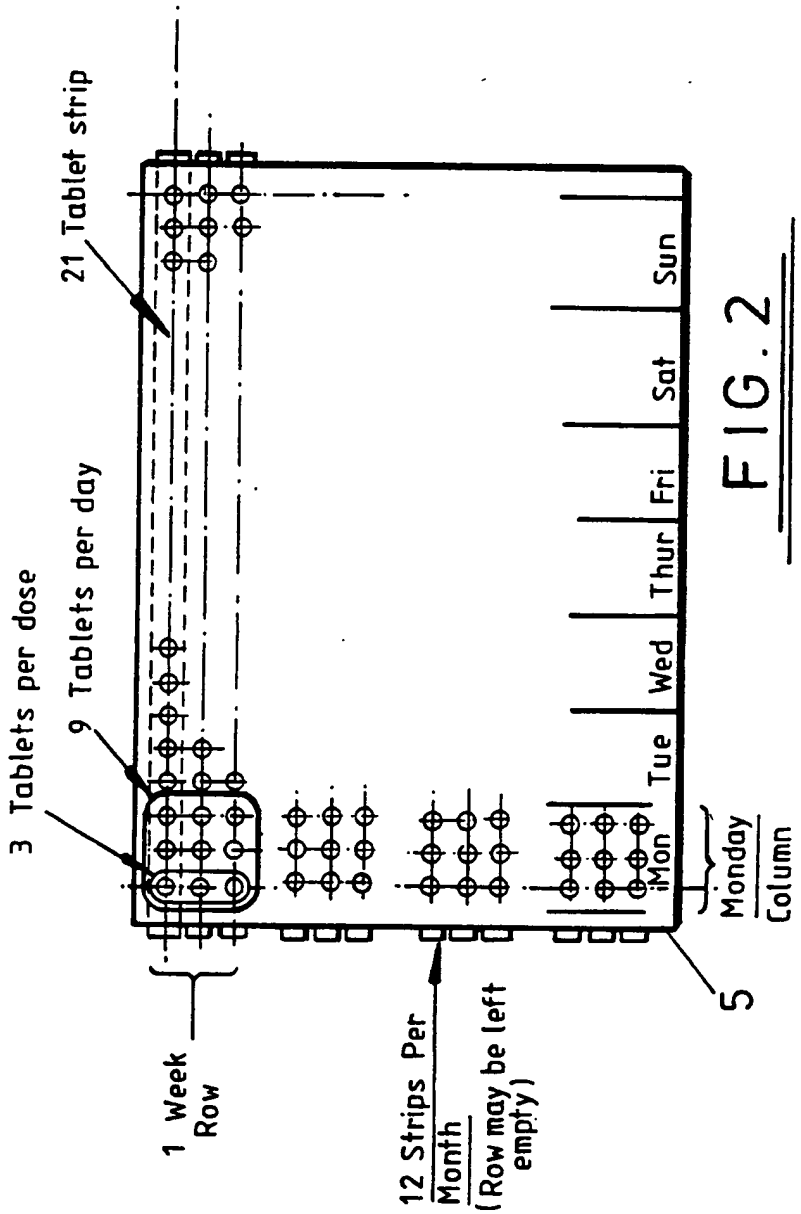

21 Tablet strip
3 Tablets per dose
9 Tablets per day
1 Week Row
12 Strips Per Month (Row may be left empty)
Mon
Tue
Wed
Thur
Fri
Sat
Sun
Monday Column
5

FIG. 2

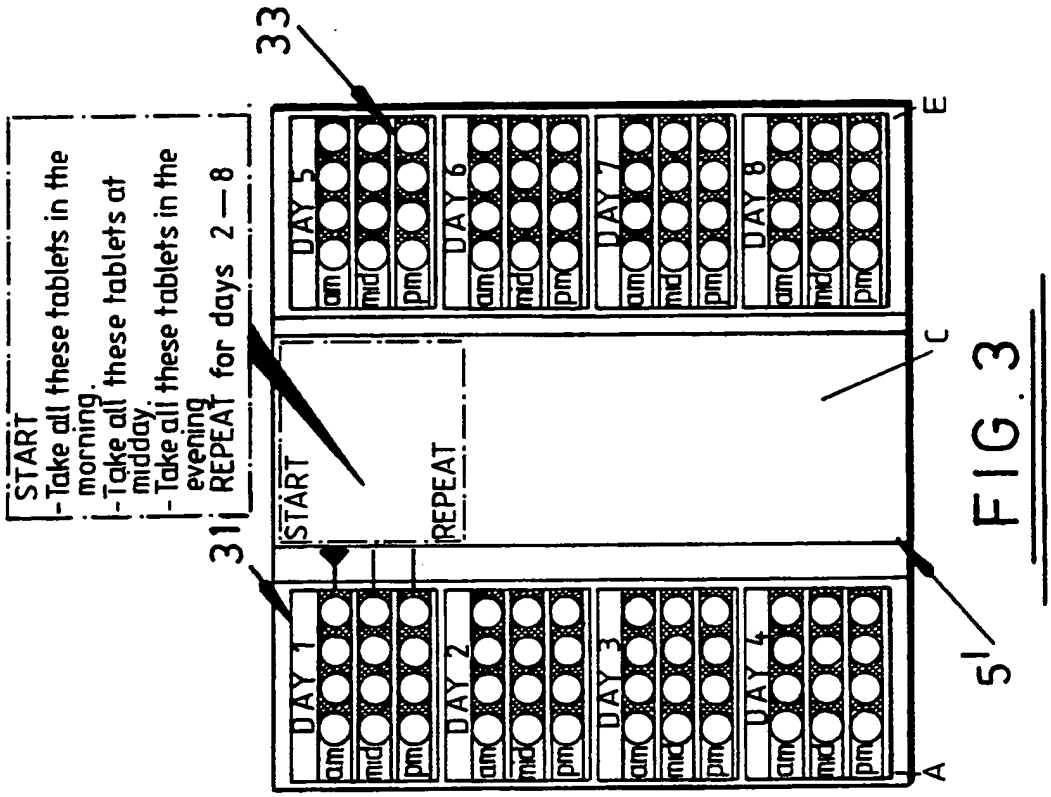

START
-Take all these tablets in the morning.
-Take all these tablets at midday.
-Take all these tablets in the evening
REPEAT for days 2—8
31
33
START
REPEAT
DAY 1
DAY 2
DAY 3
DAY 4
DAY 5
DAY 6
DAY 7
DAY 8
am
mid
pm
A
C
E
5'

FIG. 3

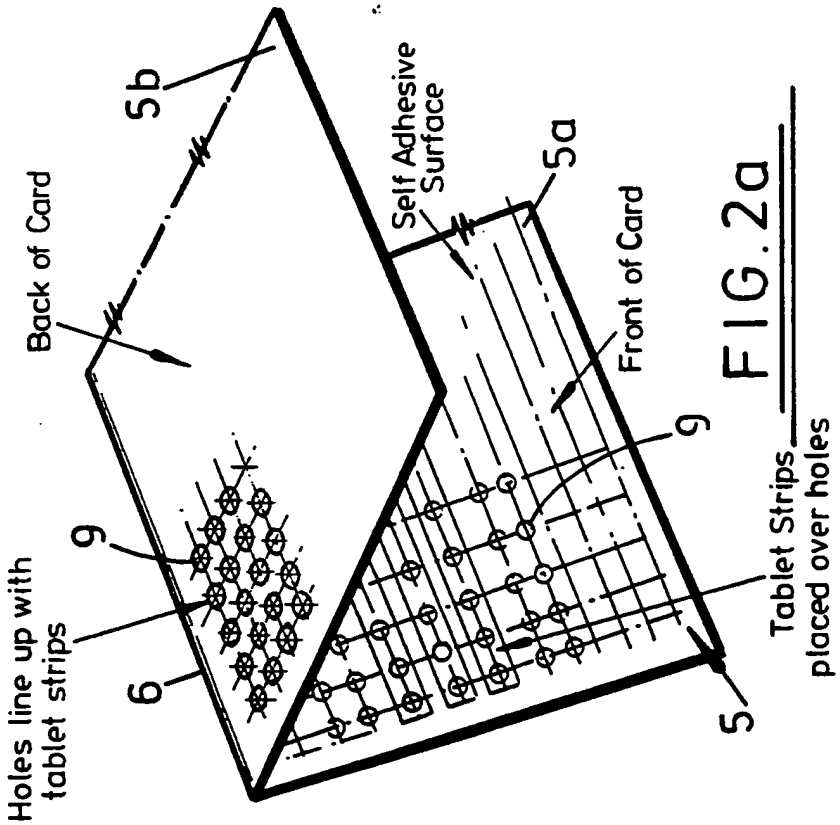

Holes line up with tablet strips
9
6
Back of Card
5b
Self Adhesive Surface
5a
Front of Card
9
Tablet Strips placed over holes
5

FIG. 2a

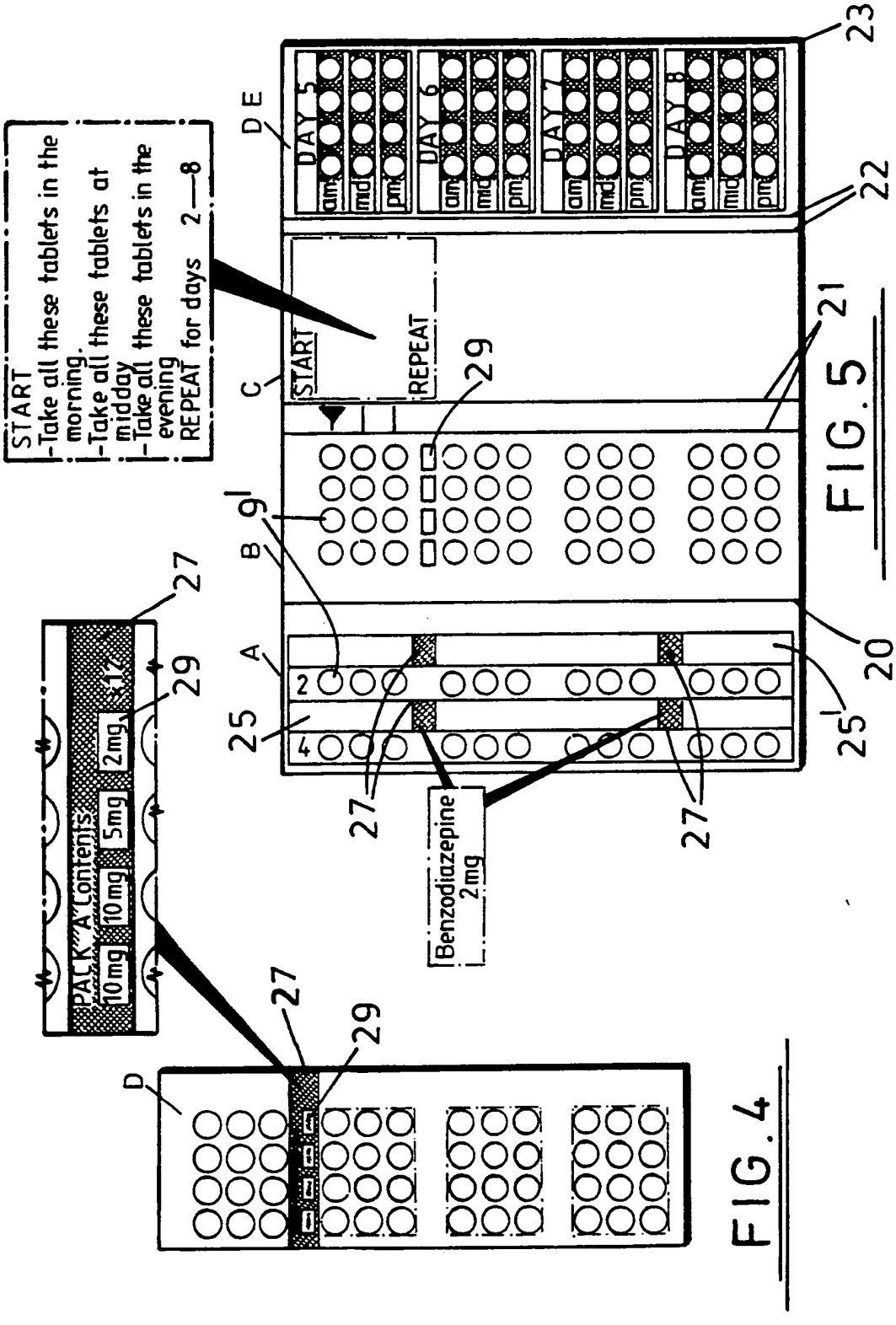

START
-Take all these tablets in the morning.
-Take all these tablets at midday
-Take all these tablets in the evening
REPEAT for days 2—8
DAY 5
DAY 6
DAY 7
DAY 8
am
mid
pm
START
REPEAT
Benzodiazepine 2mg
PACK 'A' Contents
10mg
10mg
5mg
2mg
A
B
C
D
E
20
21
22
23
25
25'
27
29

FIG. 5

FIG. 4

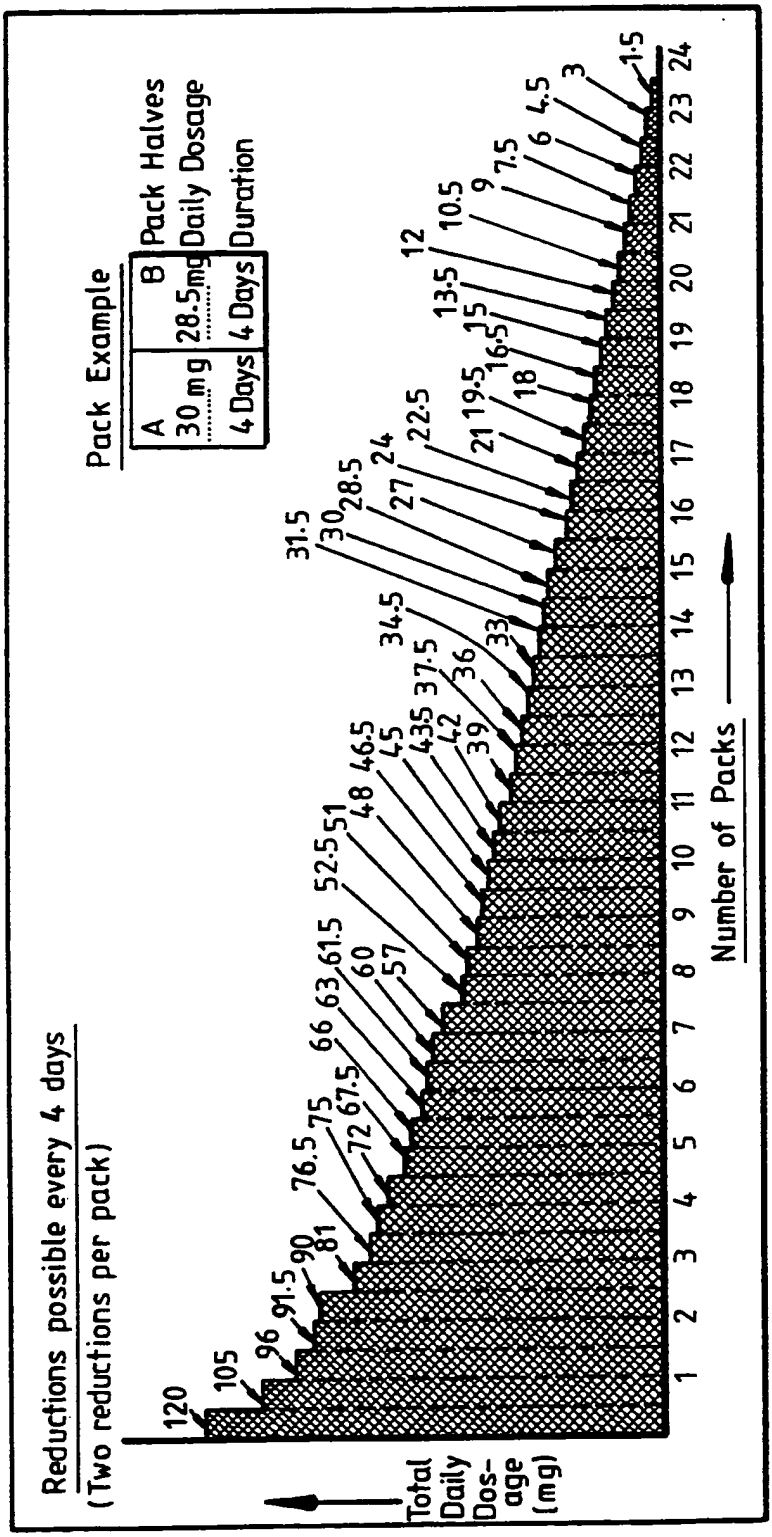

Reductions possible every 4 days
(Two reductions per pack)
Pack Example
A
30 mg
4 Days
B
28.5mg
4 Days
Pack Halves
Daily Dosage
Duration
Total Daily Dosage (mg)
120
105
96
91.5
90
81
76.5
75
72
67.5
66
63
61.5
60
57
52.5
51
48
46.5
45
43.5
42
39
37.5
36
34.5
33
31.5
30
28.5
27
24
22.5
21
19.5
18
16.5
15
13.5
12
10.5
9
7.5
6
4.5
3
1.5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Number of Packs

FIG. 6

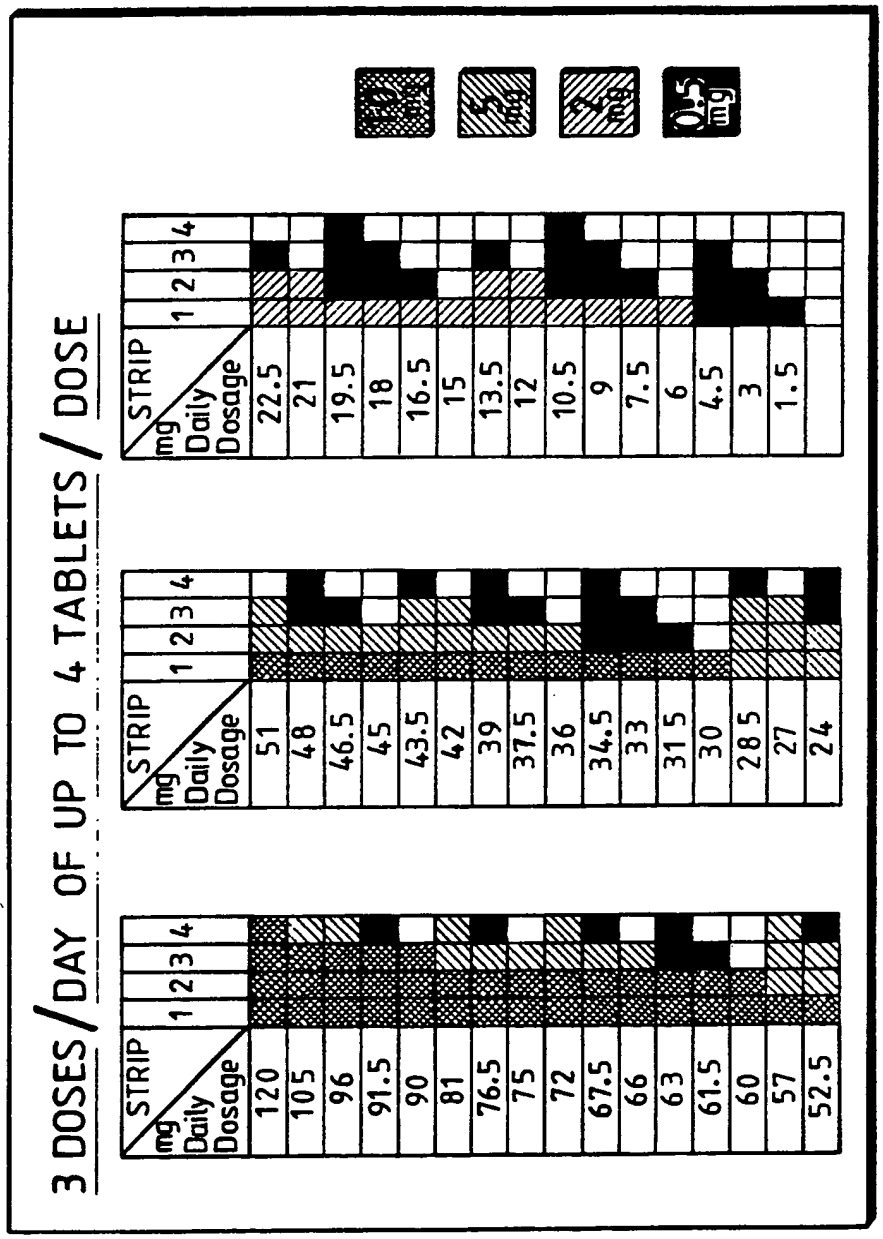

3 DOSES / DAY OF UP TO 4 TABLETS / DOSE
STRIP
mg Daily Dosage
1 2 3 4
120
105
96
91.5
90
81
76.5
75
72
67.5
66
63
61.5
60
57
52.5
STRIP
mg Daily Dosage
1 2 3 4
51
48
46.5
45
43.5
42
39
37.5
36
34.5
33
31.5
30
28.5
27
24
STRIP
mg Daily Dosage
1 2 3 4
22.5
21
19.5
18
16.5
15
13.5
12
10.5
9
7.5
6
4.5
3
1.5

FIG. 7

Title: Packaging Drugs

DESCRIPTION

The present invention relates to the packaging of medicines (drugs) and especially to medicines (drugs) taken in tablet form.

In prescribing such as tablets, it is usual for doctors to select the required dose level from generally available dose levels for the particular drug concerned and for those tablets to be taken for a given period a specified number of times per day or otherwise as specified. Where only one tablet is concerned providing a bottle/container of tablets with instructions (eg. one every five hours) is relatively straightforward. However, in prescribing for certain conditions it may be desirable to vary the dose level, or to alternate the types of tablet being taken whether on an hourly, daily or weekly basis and this creates potential problems to the patient in mixing up the prescription requirements. Furthermore, there may be cases were the dose level could be prescribed in levels which do not correspond to levels for which tablets are available and in more complicated patterns than simply

requiring the taking of two or three smaller tablets.

It is the aim of the present invention to provide packaging for medicines which affords considerable flexibility in the prescribing pattern for the medicines and yet which is easy to follow by the patient.

Accordingly, the present invention provides a package for medicines to be taken on a prescribed periodic basis, the package comprising a carrier or framework and a plurality of reception locations disposed in identifiable groupings representing single doses in relation to the carrier and wherein each grouping is made up of at least one reception location and is such as to accommodate several discrete medications (usually in tablet form) be they the same or different types and/or dose level in relation to the available capacity of each grouping.

More particularly each grouping comprises a plurality of reception locations and in that case it is preferred that each reception location serves to receive a discrete medication, although it will be understood that it is not essential to fill each of those reception locations. Indeed the number of locations filled or the number of discrete medications inserted into one larger reception location is intended

to be selectable in relation to the prescribed dose level and the available dose levels of individual tablets and/or in relation to the number of different types of medications being prescribed for each grouping. The packaging we have in mind is particularly suitable for prescribing dose levels which vary over a period of time and were the actual dose level in any one grouping can be variable in numerous steps by selecting combinations of tablets from available dose levels. For example it may be required to reduce the dose level over a several week period possibly with certain plateaus between variations and this can be readily achieved by having several tablets for each grouping which the pharmacist can assemble according to prescription and yet which the patient can easily identify as being the correct dose for that particular time or day.

According to a preferred embodiment the package comprises a carrier having a plurality of holes therein each defining said reception location and arranged in said groupings whilst the tablets are disposed in bubble pack type housings arranged on a strip with spacings of the tablets corresponding to spacings of the holes in the carrier. The carrier preferably comprises two leaves between which the strips of

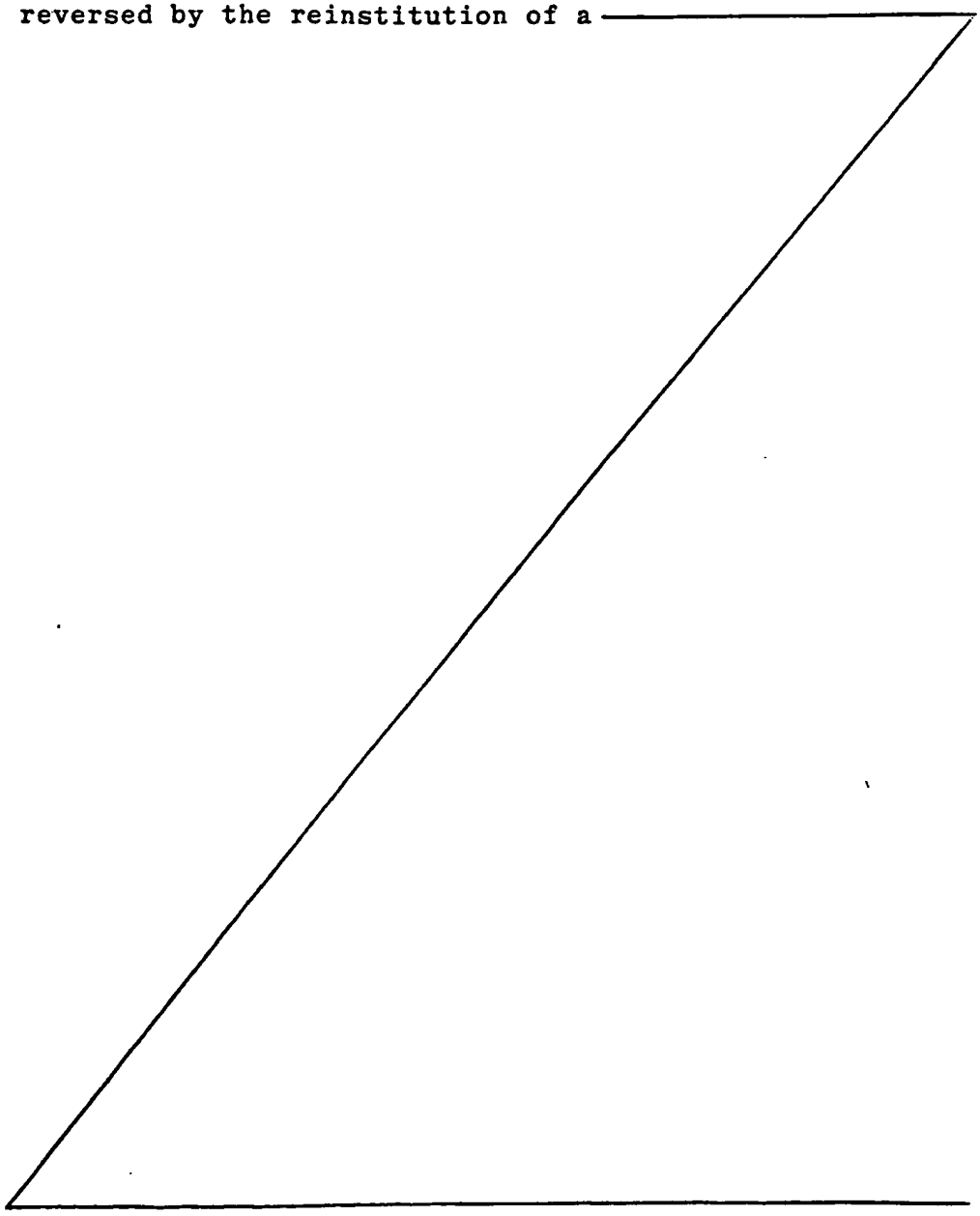
tablets can be located and positioned in the required numbers to give the required dose for each grouping. One embodiment has three reception locations to each grouping arranged in a column, which constitutes a single dose. Three or four such columns constituting the total daily dose. Another embodiment has four reception locations to each grouping arranged side by side in a row, and say three rows constituting the daily dose (eg. morning, midday and evening). The dose for a number of weeks being set out in rows or columns- preferably the former. Conveniently the pack is in two or more sections with a number of days dose (say four) to say two or more of the sections.

The present invention is particularly useful as a tranquilliser withdrawal package aimed at minimising withdrawal symptoms.

Chronic withdrawal symptoms begin between the ninth and twentieth day after abrupt cessation of the benzodiazepine. Symptoms occur primarily in the long term, high dose abuser and also in the long term therapeutic dose dependent individual, either of whom has accumulated considerable drug and metabolics. When these active substances are excreted slowly, as in the case of long-acting benzodiazipines, chronic withdrawal can be a protracted event (Covi et al, 1973).

The syndrome, which may last 15-45 days, is

characterised by increased depression, agitation, marked insomnia, severe nightmares, loss of appetite and an aggravation of pre-existing psychological distress. The syndrome represents true withdrawal, since symptoms are reversed by the reinstitution of a



benzodiazipine. (Ayd, 1983).

Counselling services have been quick to respond to this ever increasing situation. Various theraputic methods and approaches have been adopted, some are more beneficial than others. Most methods of withdrawal required co-operation from the clients General Practitioner.

Most conventional methods of "out-patient" or "self help" withdrawl programmes are client centered and can be relatively primative. The majority of Tranquilliser dependants are now aware of the afore-mentioned associated side affects. Radio, Television and the media in general have been largely responsible for alerting the public to the dangers of long term use of Benzodiazipines.

Primative client controlled withdrawal currently comprises practises that are wholly inaccurate and in some cases dangerous. A presently much favoured method incorporates the use of a match box or any abrasive material, filing particles away from the tablets irrespective of dose or substance, the objective being to gradually reduce the intake of the tranquilliser in minute quantities so that the actual withdrawal effects experienced by the user are kept to a minimum. Lorazepam (Ativan) dependants experience the greatest

difficulties, their problem is further aggravated by the limited availability of tablets of varying strengths. For instance a person dependant upon Lorazepam attempting a gradual reduction using one quarter mg steps would find accuracy extremely difficult because Lorazepam is presently only available in 1+3mg tablets. These tablets are not designed to aid a dependant person to detoxify.

In one embodiment the invention provides a method of dispensing drugs in tablet form in such a way that the amount of drug taken by the patient can be varied with the time in a precise way, thus offering the physician an extra dimension to drug therapy which until now required intensive monotoring by medical staff to achieve the same results.

The possibility of varying drug levels on a daily basis using a system that the patient can easily control (understand) which then enables the physician to prescribe a precisely tailored drug therapy to match the individual patient's requirements. Drug levels can be increased and decreased at precise rates with maximums timed to coincide with particular clinical events. Complex drug therapies requiring the administering of different dose levels of different drugs can be effectively managed by the patient

themselves. The administration of placeboes can be interspersed with active drugs without compromising their effectiveness. The ability to tailor the drug therapy in terms of dose to a particular patient and then to alter that dose level with time at a particular rate makes the system ideally suitable to the problems of managing drug withdrawal programmes for long term users. It is for this particular application that the present embodiment of the invention relates although its wider application into general drug therapy is acknowledged. Existing drug packaging systems provide some indication to the patient that the drug has been taken i.e. the female contraceptive pill being an example. Such systems have the disadvantage that they cannot be precisely targeted at particular patients in terms of their dose levels and therefore their usefulness outside the particular well-defined application is limited in terms of drug withdrawal programme application.

An ideal drug dispensing system would enable different patients to start the therapy at different dose levels offering alternative rates of reduction and would allow the physician to prescribe the exact programme of withdrawal. It would enable the pharmacist to dispense the prescribed drugs easily and

accurately and would assist the patient to follow the withdrawal programme safely and without difficulty. It would also enable the manufacturing drug company to supply the necessary product to meet these criteria as cheaply as possible using existing technology.

In the case of Diazepam (Valium) withdrawal daily dose levels can vary dramatically, high doses are not uncommon nor is long term prescribing. Both these variables are important in determining the optimum withdrawal programme. Diazepam is currently available in 2mg, 5mg and 10mg tablets. The invention describes a method by which these tablets can be easily dispensed to a particular regime and the regime can be easily followed by the patient. The system requires that the pharmeceutical company continue to manufacture Diazepam in the current 10mg, 5mg and 2mg tablets and to package these tablets in blister packs in the form of a single strip of for example, 21 tablets giving a three times a day dose for one week.

A dispensing card designed to hold the tablet strips in a particular sequence so that various tablet combinations can be presented to the patient at particular times, is also included. The dispensing card is pre-punched with holes to accept the tablet strips which the pharmacist will load according to the

prescription. The card enables up to three tablets to be taken safely as a single dose 3 (or 4) times a day. A typical card would contain sufficient tablets for a convenient period of time say 7, 14, 21 or 28 days, with a single day providing for up to nine tablets to be taken in three separate doses. As all the horizontal holes of a particular row are filled with tablets of the same strengths a single strip being laid across the card, dose levels are built up by varying the following two tablets in the column. All dose levels in any week are the same, but dose levels from week to week can be varied depending on the combination of tablet strips used. Further flexibility in prescribing levels arises from the introduction of tablets of 0.5mg.

The present invention will now be described further by way of example only with reference to the accompanying drawings; in which:-

Figure 1 is a plan view of a strip of 21 tablets;

Figure 2 is a simplified plan view of a package according to the invention incorporating a selected number of strips of Figure 1;

Figure 2a is a perspective view of a package showing how the strips of Figure 1 are incorporated into the package;

Figure 3 is an inside view of another embodiment of package;

Figure 4 is an external view of one of the sections of the package of Figure 3;

Figure 5 is an internal view of the package of Figures 3 and 4 showing one section opened up;

Figure 6 is a bar graph showing flexibility in prescribing levels, and

Figure 7 is a chart showing the strips required to make up the desired dose level.

Figure 1 shows a strip of 21 tablets 1 in a blister pack 3 which would be sufficient for a three times a day dose for seven days. The strength of the tablets will conform to those currently available from the manufacturers, and all tablets in a particular strip will be of the same strength. Strips of tablets of different strengths could be colour coded.

Figure 2 and 2a shows a package made up of a carrier 5 illustrated as having two leaves 5a, 5b hinged at 6 to accept a plurality of blister packs of tablets 3. The carrier has holes 9 formed in both leaves to be in alignment when folded. The strips 3 can be fitted into the carrier in rows (the blisters being spaced to conform with the spacing of the holes 9) with the number of strips inserted being determined by the prescription requirement. The carriers have a self adhesive coating for holding the tablets in position when the two leaves are brought together.

The holes 9 define reception locations and are arranged in identifiable groupings in the carrier, either by spacing thereof or by printing the form of lettering and/or colours. In the illustrated embodiment, the groupings comprise three rows and three columns giving nine reception locations to each groupings. Those groupings can be disposed side by side to provide a weeks prescription and/or in rows of weeks - say for a months prescription or longer if required. Figure 2 shows the groupings for four weeks, with provision for three tablets three times per day.

The alternative embodiment described with reference to Figures 3 to 5 comprises a carrier 5' of suitable material having five sections A to E defined by fold lines 20,21,22,23. Sections A,B and D,E have through holes 9'. Tablets are supplied in strip form as blister type packs with spacings of the blisters corresponding to the spacing of the rows. Thus the required number of strips are fitted as columns to sections A and E. Two strips are shown at 25,25' in Figure 5 applied to section A. Once in place the section A is folded to overlie section B and similarly for section D and E. The right hand side of Figure 5 shows the two sections D,E folded. Figure 3 shows sections A,B and D,E folded. Thus the strip is trapped between the two sections. The strips have a rupturable

backing which facilitates extraction of the tablet contained in the blister by way of the original aperture in the underneath section eg. B or D as the case may be. The backing strip also carries data card 27 as to the strength of the tablets enclosed in the blister and this information is visible through aperturing 29 in the sections B and D (see Figure 4). The data is preferably colour coded ie. each strength of tablet has a different colour code.

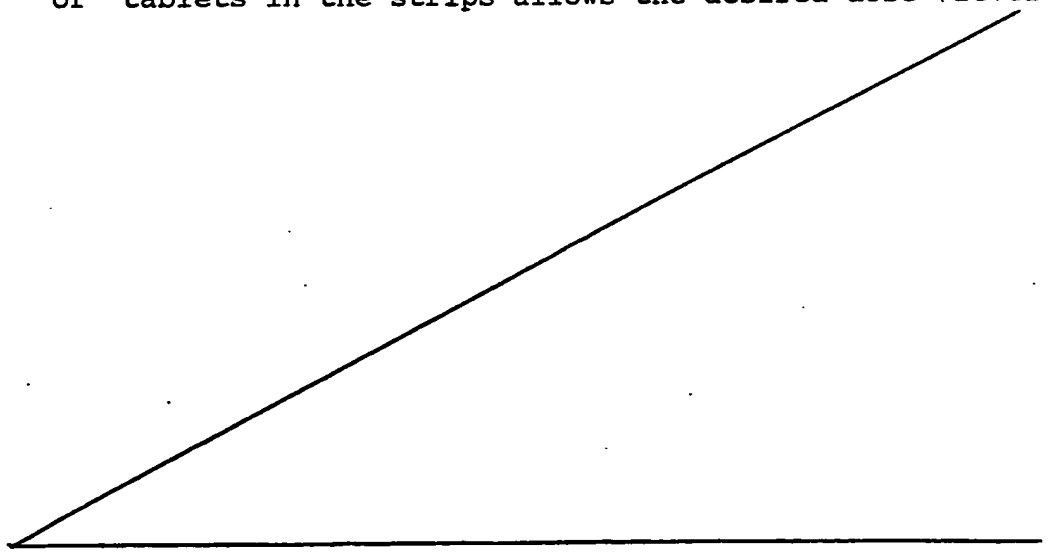
In this embodiment each grouping comprises four reception locations ie. aperture 9' making up the desired dose level, and with facility for 3 doses per day eg. morning, midday and evening. The illustration has four days to each of parts 31,33. Part 33 can be folded over section C and part 32 over that to form a neat pack - say for accommodation in a box.

A Doctors Prescribing Aid is proposed in the form of a visual bar graph (see Figure 6). This highlights the possible system dosage alternatives for use in the event of reducing a persons drug intake over time (withdrawal) based on the use of 4 drug levels - namely 10mg, 5mg, 2mg or 0.5mg. This shows the daily dosage options based on 3 doses/day using up to 4 tablets/dose with patient pack which comprises two halves offering a 4 day course/half, each half can hold differing dosage levels where the tablets are provided in strip form.

To assist prescribing, and to rationalise the doctors information to the pharmacist, it is proposed that a pre-printed sheet be completed giving the dose required for each half A and B of the pack and for each of a numbered sequence of packs.

Upon receipt of the doctors pre-printed sheet giving the dose for A and B (see inset to Figure 6), the pharmacist matches the prescribed dosgage against a packaging chart (see Figure 7) which breaks down the dosage into the make-up of strips (10mg, 5mg, 2mg or 0.5mg). Different daily dosage options would be obtainable if the doses were 1/day or 2/day, hence differing charts would be required. The strips would be colour coded in the final printed version of this dispensing aid.

Selection of the member of strips and the value of tablets in the strips allows the desired dose level



to be prescribed. With this embodiment the dose level to parts 31 and 33 may be different.

It will be understood that the number of strips inserted for each day i.e. 1, 2 or 3 will be determined by the required dose level and the available tablet dosage. Described hereinafter are the possible dose variations for a nine tablet per day programme (3 x 3 tablets per day) assuming 10mg, 5mg and 2mg tablets are available.

Week No.	Daily Dose (mg)	Difference (mg)	Single dose (mg)	Difference
1	90		30	
2	75	15	25	5
3	66	9	22	3
4	60	6	20	2
5	51	9	17	3
6	42	9	14	3
7	36	6	12	2
8	30	6	10	2
9	27	3	9	1
10	21	6	7	2
11	18	3	6	1
12	15	3	5	1
13	12	3	4	1
14	6	6	2	2

15	0	6	0	2

For a twelve tablet per day programme (4 tablets taken 3 times per day) the following combinations are possible:-

Week No.	Daily Dose (mg)	Difference (mg)	Single Dose (mg)	Difference
1	120		40	
2	105	15	35	5
3	96	9	32	3
4	90	6	30	2
5	81	9	27	3
6	75	6	25	2
7	72	3	24	1
8	66	6	22	2
9	60	6	20	2
10	57	3	19	1
11	51	6	17	2
12	48	3	16	1
13	45	3	15	1
14	42	3	14	1
15	36	6	12	2
16	33	3	11	1
17	30	3	10	1
18	27	3	9	1
19	24	3	8	1

20	21	3	7	1
21	18	3	6	1
22	15	3	5	1
23	12	3	4	1
24	6	6	2	2
25	0	6	0	2

Daily levels and weekly reductions can be altered depending if the system is designed around three or four doses per day and three or four tablets per dose.

The advantage of the systems is that any of the above dose levels can be easily prescribed and the pharmacist can simply make up the appropriate dispensing card by laying either a 10mg, 5mg or 2mg strip in the appropriate row on the card or leaving that row empty. Once the correct prescription has been dispensed, the card is closed firmly holding the tablets in their correct sequence according to the prescription.

The packaging system is advantageous because:-

1. Our system would gradually withdraw dependants of short acting and long acting Benzodiazepines or other drugs irrespective of individual doses or levels of consumption.

2. The practitioner or presciber can, dependant upon their assessment of the patient, choose the appropriate

withdrawal regime that will meet the requirements of the practitioner and more importantly the individual patient.

i.e. if the presenting patient is requesting advice on withdrawal and to that date receiving maintainance or long term prescriptions of a short acting Benzodiazepine (Lorazepam, Temazepam etc) the practitioner would if he/she was to follow current medical belief, prescribe an equivalent dose of a longer acting alternative. Presently the most appropriate substitution is Diazepam. With implementation of our device, the practitioner could then prescribe a withdrawal programme tailored to the individual needs of the patient and ensure that the patient understands the administration of the reduction regime, and because of the simplicity of the device is well able to follow medical instructions.

3. Following the practitioners assessment and decision of the appropriate withdrawal regime the patient would then attend his local pharmacy for the dispensing of the prescription using our system. The pharmacists, using the device, would make up the prescription to the practitioners specifications.

4. In addition to the application of drug withdrawal

described above, the system of the invention would also be appropriate to initial therapy involving tranquilisers or other drug types that require a high initial dose reducing with time or vice versa. Such a therapy in the case of addictive drugs would be far less likely to produce dependance in the patient.

CLAIMS

1. A drug package for a drug to be taken on a prescribed periodic basis, the package comprising a carrier or framework and a plurality of reception locations disposed in identifiable groupings representing single doses in relation to the carrier, and wherein each grouping is made up of at least one reception location as is such as to accommodate several discrete medications in relation to the available capacity of each grouping and in which the dose level of the discrete medications making up said grouping is/are selected from different available dose levels to build up a prescribed single dose for that grouping.

2. A package as claimed in claim 1 in which each grouping comprises a plurality of reception locations.

3. A package as claimed in claim 2 in which each reception location accepts one of said discrete medications.

4. A package as claimed in claim 3 in which the dose level of the medication of at least two of the reception locations of each grouping have different values.

5. A package as claimed in any one of claims 1 to 4 in which the discrete medications are arranged on a strip with the spacings of adjacent medications corresponding to the spacing of adjacent groupings or

multiples thereof.

6. A package as claimed in claim 5 in which each strip has a discrete medications of a specific dose level.

7. A package as claimed in any one of claims 1 to 6 in which the carrier has a plurality of holes therein each defining said reception location.

8. A package as claimed in any one of claims 1 to 7 in which at least two groupings have different prescribed single doses.

9. A package as claimed in claim 8 when appendent to claim 6 in which the different prescribed single doses are arrived at by the use of strips having different dose level and/or by having a different number of strips to the grouping.

10. A package as claimed in any one of claims 5 or 6 in which the carrier comprises two overlying leaves each having holes corresponding to the reception locations and between which the strips of medications are located.

11. A drug package as claimed in claim 6 in which dose levels are selected from strips of 10mg, 5mg, 2mg or 0.5mg.

12. A drug package constructed and arranged substantially as hereinbefore described with reference to and as illustrated in the accompanying drawings of

Figures 1, 2, 2a or Figures 3, 4 or 5.

Published 1990 at The Patent Office, State House, 66 71 High Holborn, London WC1R 4TP. Further copies may be obtained from The Patent Office Sales Branch, St Mary Cray, Orpington, Kent BR5 3RD. Printed by Multiplex techniques ltd. St Mary Cray, Kent, Con. 1/87